S.Michele Aug.12,1956

Dear Joshua,

Both your jumbo postcard(which,as you know,we always enjoy very much )and your letter reached me in Milan,just back from the Copenaghen congress.I have been playing a little with problems in human genetics;as soon as the paper I gave there will be duplicated I will send you a copy and will hope for your comments on it.

I was very pleased to hear that your interest in transductional linkage extends beyond your note to MGB. I have enjoyed writing papers jointly with you across the Atlantic and would welcome another opportunity.I don't forget that we are always supposed to be writing a book jointly; but a joint paper has the advantage of being shorter ,so that it is of some relief to think that at least the paper may be finished soon. Perhaps it is not too bad,on the other hand,that the book is somewhat delayed;things of interest in the field are cropping up(e.g.,the pseudocholinesterase story;a polymorphism for primaquine tolerance,a new antimalarial drug,etc.) and although this principle genetics of penicillin production cannot be taken to its limit, it is good to see that as time goes by chapters that might a short time ago have been a little too thin are getting "plumper".

My suggestion is that we may write a joint paper,say for AM. Nat.as you suggest ,on transductional linkage,and personally,I would like you to take senior authorship in it and use as much of the stuff of the paper in your hands(possibly all,if necessary in abridged form)as you deem useful.Although I am not,myself,fully convinced of the random breakge theory,I think it is useful to have at least its expectations set out clearly.On the other hand,I feel it a rather difficult job to distinguish between random termini and fixed termini;and,in suggesting you take senior authorship ,I am disguising the hope that you have good suggestions as to the ways in which the various hypotheses, so well listed by yourself,can be disentangled one from the other when one comes to the testing of them . I hope this plan suits you,even if it may be difficult at this stage,to give rigorous criteria to distinguish between the various hypotheses. I think the paper would also be a good opportunity for unraveling some of the confusion now existing in the heads of so many geneticists and non-geneticists as to the mechanisms of crossing over; some people seem to think it absolutely certain that e.g.the Levinthal model cannot apply to Drosophila,and I am not quite sure that this is correct. In any case,I am confident that writing the paper will clarify my own ideas on the subject.Therefore I hope you will accept the plan. My proposed junior authorship does not necessarily mean that I am planning to be a passive observer of what you will write.I suppose that even of my contribution were only one of a discussant,the subject is sufficiently tough to make it worth the while. Should the plan not suit you, however,we may always publish our papers in a correlated way. Mine would certainly need some rewriting,e.g. I have been using the same symbols for genes and for distances,which is confusing;there is some exchange between n and m inthe paper,and various other things. More important:I have been criticised for the assumption that the number of breaks is high,but if all there is in it I think is that the number of breaks per chromosome must be high,not the number of breaks per crossover(which in fact turns out be small,but is not important forthe theory) and I have not made the distinction sufficiently clear perhaps. It has also been suggested that perhaps the fact that the ratio crossover/break turns out to be not far from unity may be biologically significant .This has struck me as an interesting consideration,though at the moment I am rather unaware of how far it may lead.

The ideal would be, I think, to touch adequately the following points:

1) proposed mechanisms for crossing over (in general) if nothing else, to xxxx2) xxadditionnal state that they may be immaterial to the problem;

2) special hypotheses for transduction: the mode of fragmentation and transfer of fragments;

3) the genetical consequences of each model;

4) a discussion of whatever data are available, and of how to collect the data for testing the hypotheses.

5) relations to other models of inheritance, e.g. recombination in K-12, interference pattern in Aspergillus, anything else ?

As to your worries about the word transduce and its use; I am obviously no authority in English, but the verb has probably not been used often before you, and your use with a double object perhaps is not so objectionable. On the use of the word transduction in connection with DNA transformation I am not completely agreed. It is true that the same genetical theory may hold fo both, but the distinction xxxthe due to a specific carrier, phage in one case none or X in the other, calls to my view for different names, or at least sub-names. In any case, I think the word transformation will still be largely use and there is no great hope that it will fall out of use soon; you will undoub thy add to its use of you say that "mutant (?) clones are transformed by phage which transduces fragments to them". Although I never have strong views on terminology, except when it gets really confusing (and I think nothing of this has yet happened in microbial genetics), I am still a little unsatisfie with the words "heterogenotes, exogenotes" as they imply an identity xxthe between fragments and genes which might be occasionally correct (lambda?) but in most cases, even with the loosest definition of gene, is not granted. I am tentatively, and very shily, proposing an alternative name to include partial heterozygotes in K-12 and heterogenotes, xxxxxxx namely "merozygotes"; "merohybrids" also might do. I am also wondering if one can use the word hybridise (as one would with fertilise) in the passive form, to substitute for *transform in the sentence above. In any case I would substitute segregant for mutant. Perhaps xx the best would be to avoid a sentence xx in the exact form as you gave it. But nothing of this is really important, perhaps.

We are planning to go the the Ciba symposium and, when spending a few days in London just before the Copenaghen congress it was very pleasant to know that you/xxso too might be there. However, I hope this will not decrease the chances of a visit of yours to Italy. Either before or after the Ciba; or in September, if you come back the same way. Another thing about your proposed trip : Westergaard is very anxious to see you in Copenaghen, and perhaps it may be easy for you to call there. I assume that if you fly all the way round the world it may be easy for you to stop any place in Europe free of charge, even with a little zig-zagging South and North; it may also help financially. Although the situation has unfortunately been sofar a poor one, at home, I will see what can be done xxxxxxx about lecture fees, etc.

All the best to you and Esther, also from Alba. Did I write you that the family is increasing? We are well above average Italian birth rate now. Perhaps the planning was a bit careless, considering that I am fed up with the place where I am working, and the present family condition limits our movement greatly for the next months or even for the next year. Unfortunately the routine work has increased so much that it leaves very little time for thinkin of my own problems. It will be convenient to have our joint book finished befo

Long, so that if nothing better turns up here soon, the book may help to have my way to the States. If you could get your lectures outlined before you leave for Australia, I think it could be ready by the time you come back! All the best yours Luca!